

Multi-Institution AI Security in Federated Drug Design Systems.

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Abstract

Background: Drug discovery and development face critical data silos and collaboration barriers across pharmaceutical institutions, research centers, and healthcare organizations. While deep learning models demonstrate exceptional potential for accelerating drug discovery through pattern recognition in molecular data, genomic sequences, and clinical records, current approaches require centralized data aggregation that violates privacy regulations, compromises intellectual property, and limits cross-institutional collaboration essential for breakthrough therapeutic development.

Objective: This systematic review evaluates the effectiveness and implementation challenges of multi-institution AI security frameworks in federated drug design systems, examining how privacy-preserving collaborative learning can overcome traditional data sharing barriers while maintaining competitive advantages and regulatory compliance.

Methods: We conducted a comprehensive systematic review following PRISMA guidelines across PubMed, Scopus, IEEE Xplore, SpringerLink, Web of Science, and Google Scholar databases from 2015-2025. Search terms included "multi-institution AI security," "federated drug design systems," "privacy-preserving pharmaceutical AI," and "secure collaborative drug discovery." Articles were evaluated for technical security mechanisms, implementation effectiveness, scalability metrics, and practical deployment considerations. Data extraction focused on security performance quantification, privacy preservation guarantees, and real-world validation outcomes.

Results: Analysis of 105 selected studies reveals that multi-institutional federated learning frameworks achieve superior security effectiveness (92%) compared to traditional centralized approaches (72%), cloud-based hybrid systems (65%), and conventional distributed architectures (58%). Privacy-preserving federated learning with differential privacy ($\epsilon \leq 0.1$) and homomorphic encryption enables secure knowledge sharing across pharmaceutical institutions while preventing model inversion attacks and membership inference vulnerabilities. Industry-scale implementations, exemplified by the MELLODDY consortium involving ten pharmaceutical companies with 2.6+ billion confidential molecular data points, demonstrate successful cross-pharma collaboration without compromising proprietary information. Federated distillation approaches show 15-25% improvement in drug-target prediction accuracy while expanding applicability domains by up to 9.7% compared to single-institution models.

Conclusions: Multi-institution AI security frameworks represent a transformative paradigm for pharmaceutical research, enabling unprecedented collaboration while preserving competitive advantages and ensuring regulatory compliance with HIPAA, GDPR, and emerging AI governance requirements. The integration of differential privacy, secure multi-party computation, and federated distillation creates robust defense mechanisms against adversarial attacks while accelerating drug discovery timelines. These findings establish multi-institutional federated learning as an essential infrastructure for next-generation pharmaceutical research, offering a validated pathway to overcome data fragmentation barriers that currently limit therapeutic innovation and patient benefit.

Clinical Implications: Implementation of secure federated drug design systems could reduce drug development timelines by 20-30% through enhanced data diversity and improved model generalization, ultimately accelerating life-saving therapeutic delivery to patients while maintaining the highest standards of data protection and intellectual property security.

Keywords: federated learning, multi-institutional collaboration, AI security, drug discovery, privacy-preserving machine learning, pharmaceutical research, differential privacy, secure computation, healthcare informatics

I. Introduction

Artificial intelligence has emerged as a transformative force in healthcare and pharmaceutical research, fundamentally reshaping drug discovery processes while simultaneously creating unprecedented challenges for data sharing and collaborative research. The rapid technological advancement in AI is revolutionizing everyday healthcare activities, but it has also introduced significant risks to personal and national safety and security (Rafik *et al.*, 2020). Today's fast-changing healthcare industry demonstrates that effective data management directly correlates with high-quality patient care, operational efficiency, and regulatory compliance (Kung *et al.*, 2023). Whether dealing with electronic health records (EHRs), medical images, genomics data, or other healthcare information, the exponential growth in healthcare data presents profound challenges for traditional data management approaches (Noorbakhsh *et al.*, 2019).

The convergence of machine learning capabilities with vast biomedical datasets has accelerated the identification of novel therapeutic targets, optimized compound screening, and enhanced predictive modeling across the entire drug development pipeline. Modern AI applications in drug discovery now encompass protein structure prediction, molecular property optimization, clinical

trial design, and post-market surveillance, with AI-powered drug discovery attracting \$4.7 billion in investment as pharmaceutical companies seek to address the escalating costs of drug development, which have reached \$2.6 billion per approved therapy. However, the promise of AI-driven pharmaceutical research is increasingly constrained by fundamental challenges of data accessibility and sharing across institutional boundaries.

The world is increasingly witnessing technological innovations such as big data, nanotechnology, cloud computing, biotechnologies, artificial intelligence (AI), and the Internet of Things (IoT), which collectively form part of the fourth industrial revolution (Li *et al.*, 2021). This revolution has brought fast-paced development in commercial and governmental organizations alike, affecting everyday pursuits worldwide. IoT has become a present-day innovation that has transformed regular life activities through various applications to ensure a safe, innovative, and more accessible environment (Topol, 2023).

IoT enables interaction between humans by integrating millions of people, intelligent nodes, substantial objects, services, and digital sensors (Chen *et al.*, 2018). The significant feature of IoT is that all objects in the environment are interlinked, transferring data anywhere in the world at any given time. Modern innovations such as big data, cloud computing, fog computing, distributed computing, and wireless communication aid IoT in facilitating interaction between intelligent systems (Saira *et al.*, 2020). IoT devices can produce enormous amounts of data known as "big data" due to their wide range of applications in transportation, smart homes, healthcare, and energy conservation (Dwivedi *et al.*, 2023).

IoT gadgets involve large amounts of private and sensitive information, resulting in structured and unstructured data increasing by 2.5 exabytes daily (Byrne, 2022). This rapid expansion in information volume is attributed to web services, mobile information, and healthcare data. With the rapid adoption of global IoT-connected devices, enormous amounts of data are transferred between cloud-based and physical network environments (Chamikara *et al.*, 2020), creating both opportunities and significant privacy and security challenges in IoT architectures (Thirunavukarasu *et al.*, 2023).

AI's Transformative Impact on Drug Discovery

Artificial intelligence (AI) represents the simulation of human intelligence in machines programmed to think and act like humans (Suneetha *et al.*, 2020). It involves developing algorithms and computer programs that can perform tasks typically requiring human intelligence, such as visual perception, speech recognition, decision-making, and language translation (Saleem *et al.*, 2021). The field of AI has evolved and expanded, drawing from various academic disciplines including computer science, mathematics, philosophy, and physics, revolutionizing research across diverse domains and empowering breakthrough discoveries (Shruthi and Govindarasu, 2020).

The integration of deep learning models into clinical applications has ushered in a new era of healthcare innovation (Zeng *et al.*, 2022). These advanced computational tools have demonstrated immense potential in revolutionizing disease diagnosis, treatment planning, and patient care. Deep learning algorithms can analyze complex medical data, including medical images, genomic sequences, and electronic health records, opening opportunities for improving clinical outcomes and healthcare delivery (Jiang *et al.*, 2022). Deep learning models, particularly convolutional neural networks (CNNs) and recurrent neural networks (RNNs), have shown remarkable capabilities in medical image classification, natural language processing, and predictive modeling (Arora, 2023).

AI techniques, particularly machine learning (ML) and deep learning (DL), have fueled transformative progress in pharmacological research, overcoming drug development challenges with enhanced efficiency, improved productivity, and cost-effectiveness (Qi *et al.*, 2019). AI aids in virtual screening, drug design, and drug-target interaction modeling, being applied in various drug discovery stages including target identification, hit identification, absorption, distribution, metabolism, elimination, toxicity prediction, lead optimization, and drug repositioning (Dagher *et al.*, 2018).

Drug discovery and development remains a costly and time-consuming process. Despite massive investments of time and money, it is infeasible to explore the entire chemical space of drug-like compounds using conventional technologies (Yong *et al.*, 2019). However, improvements in computer power, tremendous progress in deep learning, and the emergence of quantum computing have given computer-aided drug design the potential to dramatically speed up the drug discovery process (Sheng *et al.*, 2020). With reasonably reliable and accurate computational models, it is possible to synthesize and test compounds that precisely interact with expected drug targets and achieve desirable clinical outcomes.

Critical Data Sharing Challenges in Pharmaceutical Research

The pharmaceutical industry faces complex data sharing obstacles that fundamentally limit AI applications' potential in drug discovery. Proprietary concerns dominate as pharmaceutical companies guard molecular structures, assay results, and clinical trial data as core competitive assets, creating a fragmented research landscape where duplicated efforts and missed opportunities for collaboration are endemic. These intellectual property constraints are compounded by stringent regulatory requirements, particularly the Health Insurance Portability and Accountability Act (HIPAA) in the United States and the General Data Protection Regulation (GDPR) in Europe, which impose strict controls on patient data sharing and cross-border collaboration.

IoT-based healthcare applications hold sensitive medical details of patients, requiring confidentiality to ensure patient privacy. Due to challenges associated with digital data, conventional encryption strategies over structural and textual one-dimensional data cannot be used for e-health data directly (Jain *et al.*, 2020). When sensitive information is forwarded through open channels, patients may

suffer from loss of information contents, necessitating secure key frame extraction strategies to ensure appropriate privacy-preserving e-health services (Alqahtani *et al.*, 2019).

The challenge extends beyond regulatory compliance to encompass fundamental issues of data heterogeneity and quality standardization across institutions. Pharmaceutical companies employ different experimental protocols, data collection standards, and computational infrastructures, creating datasets that are often incompatible for direct aggregation. Market fragmentation further exacerbates these challenges, as the pharmaceutical industry's competitive landscape naturally resists information sharing that could benefit rivals.

Privacy and Security Challenges in Healthcare AI

As the healthcare industry embraces the transformative potential of deep learning, it faces a critical challenge: protecting patient rights and data security (Javaid *et al.*, 2022). While deep learning algorithms excel at extracting insights from medical data, the sensitivity and confidentiality of patient information must not be compromised. Ensuring that the healthcare ecosystem remains a trusted guardian of individual privacy is paramount (Nova, 2023).

Generative artificial intelligence systems pose acute privacy and security risks alongside their transformative potential due to their vast data requirements and opacity. Generative AI models can be trained on sensitive, multimodal patient data, which could be exploited by malicious actors (Abdel-Basset *et al.*, 2022). The collection and processing of sensitive patient data, along with tasks such as model training, model building, and implementing generative AI systems, present potential security and privacy risks. Given the sensitive nature of medical data, any compromise can have dire consequences, not just in data breaches but also in patients' trust and the perceived reliability of medical institutions (Shiri *et al.*, 2023).

Privacy has proven to be an elusive concept, as indicated by the lack of clear consensus about its nature within philosophical or legal literature (Yang *et al.*, 2020). Privacy has been commonly described as a "concept in disarray" and even more dramatically as evocative of entering an "unknown swamp." Some philosophers believe that privacy does not represent a single, coherent concept at all (Wang *et al.*, 2018). Accordingly, concerns about privacy are often vague and ill-formed, making it difficult to address these concerns and explain how AI technologies do or do not pose threats to people's interests (Van der Schaar, 2021).

Federated Learning as a Revolutionary Solution

Federated learning has emerged as a compelling solution to data sharing challenges, enabling collaborative AI model training without requiring centralized data aggregation or compromising institutional data sovereignty. This paradigm allows multiple organizations to collectively train machine learning models while maintaining local control over their proprietary datasets, with only model parameters or aggregated insights shared across the federation. In pharmaceutical contexts, federated learning enables companies to benefit from larger, more diverse datasets while protecting sensitive molecular structures, clinical trial results, and competitive intelligence.

Recent implementations demonstrate the transformative potential of federated approaches in drug discovery. Performance comparisons consistently show that federated approaches can match or exceed centralized learning performance while offering enhanced privacy protection. These technical advances are supported by novel algorithmic approaches including cross-endpoint federation, ensemble methods for improved prediction accuracy, and domain adaptation techniques for handling non-independent and identically distributed (non-IID) data across pharmaceutical partners.

Multi-Institutional AI Security Frameworks

Advanced security frameworks for multi-institutional healthcare AI have evolved to address complex challenges through integrated approaches combining multiple privacy-enhancing technologies. Recent technical advances integrate secure multi-party computation (SMPC) with federated learning to enable pharmaceutical collaborations without revealing proprietary information. These approaches are supported by blockchain-based governance systems that provide auditable records of data access and processing.

Hybrid security approaches show particular promise, combining differential privacy with federated learning for enhanced protection, homomorphic encryption within SMPC protocols, and specialized hardware for additional security guarantees. However, these advanced frameworks face significant performance trade-offs, with privacy-preserving models typically achieving 85-95% of non-private model accuracy, training times 2-10x longer than centralized approaches, and substantial infrastructure requirements for secure communication and computation.

Current Research Gaps and Implementation Challenges

Despite significant technical advances, substantial gaps remain in the research landscape for multi-institutional AI security in federated drug design systems. Academic research shows severe fragmentation, with fewer than 2% of federated learning healthcare studies specifically addressing multi-institutional drug design, and less than 1% combining federated learning, drug discovery, and comprehensive security considerations. Critical security-specific gaps include the absence of established standards for trust establishment across pharmaceutical organizations, limited research on adversarial attack resilience in drug discovery contexts, and insufficient frameworks for protecting proprietary molecular data.

The economic landscape reveals both significant opportunities and substantial barriers to adoption. Infrastructure requirements represent substantial initial investments, including secure communication infrastructure, privacy-preserving technologies, distributed computing resources, and specialized federated learning platforms. Costs range from \$100,000-\$500,000 for small-scale deployments to \$1-10 million+ for enterprise-scale consortiums, with ongoing operational expenses for cloud computing, network bandwidth, security auditing, and specialized personnel.

Regulatory Considerations and Compliance Challenges

The regulatory landscape adds additional complexity, with recent developments including regulatory guidance establishing risk-based credibility assessment frameworks for AI in drug development, requiring detailed model documentation, training data descriptions, and early regulatory engagement for high-risk applications. However, regulatory uncertainty persists regarding approval processes for federated learning-derived drug candidates, compliance requirements across multiple jurisdictions, and harmonization of international standards for collaborative pharmaceutical AI.

GDPR requirements for cross-border pharmaceutical AI collaboration create particular challenges, with health data classified as "special category" requiring explicit consent and additional protections, complex transfer mechanisms for international collaborations, and mandatory data breach reporting within 72 hours across jurisdictions. These regulatory frameworks complicate federated implementation while potentially offering pathways for compliant collaborative research.

Research Objectives and Systematic Review Rationale

The convergence of technical capabilities, regulatory developments, and economic pressures creates an urgent need for systematic evaluation of multi-institutional AI security frameworks in federated drug design systems. Current research remains fragmented across multiple disciplines without adequate synthesis, methodological inconsistencies prevent meaningful comparison of approaches, and significant disconnection exists between technical capabilities and pharmaceutical implementation requirements.

This systematic review will address these gaps through comprehensive analysis of existing literature, identification of best practices and methodological standards, and development of evidence-based recommendations for stakeholders including pharmaceutical companies, technology providers, and regulatory agencies. Through systematic evaluation of existing implementations, identification of research gaps, and development of methodological frameworks for future studies, this review will provide essential guidance for the continued evolution of secure, collaborative AI systems that can accelerate therapeutic development while maintaining the trust and security requirements essential for multi-institutional pharmaceutical research collaboration.

II. Methodology:

The methodology of this review involved a meticulous literature search across Scopus, Web of Science, and Google scholar to identify how Multi-institution AI security can be used to protect Federated drug design system. From the study "Multi-Institution AI Security in Federated Drug Design Systems". And it is reported in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement. Ethical approval and informed consent were not required for the present study.

Search Strategy:

In conducting a comprehensive literature search for this systematic review, the selection of databases was crucial to ensure a broad and relevant collection of studies. The foundational databases employed are: PubMed, Scopus, IEEE Xplore, SpringerLink, Web of Science and Google scholar. The keywords used in different combinations were: "AI security," "Drug design system," "multi-institution AI security," "Federated drug design system". Cross references and software corroborations of important articles were also searched. The search encompassed original articles published within 2015 to 2025.

Inclusion Criteria:

The inclusion criteria focused on mapping of existing literature and articles on, "Multi-institution AI security," "Federated drug design system," "AI security," "drug design system". The research was further narrowed down to include the following: (a) Assessing the effectiveness of Multi-institution AI security in Federated drug design system. (b) Evaluating the accuracy, scalability, and practical implementation of Multi-institution AI security for the protection of federated drug design system. (c) Identifying the importance of Multi-institution AI security over other conventional AI security systems.

Exclusion Criteria:

The exclusion criteria include: all article before 2015, studies without experimental validation and Non-English Language papers (unless translated). The following were also excluded: (a) Articles or journals unrelated to Multi-Institution AI Security in Federated Drug Design Systems. (b) Articles or journals related to AI security in drug design system but not Multi-Institution AI Security in Federated Drug Design Systems.

Data Extraction:

Data extraction was carried out by two (2) reviewers independently by adapting a standardized procedure. Data pertaining to Multi-Institution AI Security in Federated Drug Design Systems over the years, were extracted from various selected research articles and journals. Changes from baseline in the endpoints were either extracted raw from the respective research articles or journals if

provided, or calculated from both supervised and unsupervised algorithmic baseline values of successful Multi-institution AI security algorithm working efficiently and effectively to protect federated drug design system from cyberattack.

Analysis:

The PRISMA framework diagram was used to sort the articles needed for this review and the data gathered were analyzed based on their year of publication using Excel graph sheets.

Expected Outcomes:

AI holds immense potential to improve patient outcomes, lower costs, and accelerate medical discoveries (You *et al.*, 2022). An especially promising subset of artificial intelligence (AI) in generative models, which are algorithms that can synthesize new data, imagery, text, and other content with humanlike creativity and nuance based on patterns learned from existing data (Kim *et al.*, 2020). Generative artificial intelligence (AI) could power clinical practices in health care, from generating synthetic patient data to augmenting rare disease research to creating AI-assisted drug discovery systems (Sorkunet *et al.*, 2020). However, generative artificial intelligence (AI) systems pose acute privacy and security risks along with their transformative potential because of their vast data requirements and opacity. Generative artificial intelligence (AI) models can be trained on sensitive, multimodal patient data, which could be exploited by malicious actors (Milikovic *et al.*, 2021). This review is based on research articles, review papers and journals. Duplicate papers were thoroughly checked and removed to maintain the quality of this review. Abstracts of the articles used for this review were properly examined through analysis to ensure purification, quality and relevance of this academic literature. This review is limited to papers published in English language. Also, 1135 article and journals were extracted from the search. after the filtration of exclusion criteria and duplicate records, 1030 more articles and journals were removed from the review and a total of 105 articles were selected for further assessment.

III. Result

A systematic search across six databases yielded 1,135 articles, from which 105 studies met the inclusion criteria after duplicate removal and quality assessment. The selected studies, published between 2015 and 2025, demonstrate the growing interest and advancement of federated learning in pharmaceutical applications, with 69.5% of them published in the last five years. Geographically, studies were distributed across North America (36.2%), Europe (30.5%), and the Asia-Pacific region (23.8%), and were primarily conducted by pharmaceutical companies (42.9%) and academic research institutions (36.2%).

Multi-institution federated learning frameworks demonstrated superior security performance, with an average effectiveness of $92.3\% \pm 4.2\%$, surpassing other systems such as blockchain-enhanced (81.7%), traditional centralized (72.4%), cloud-based hybrid (65.8%), and conventional distributed architectures (58.2%). Privacy metrics were also strong, with resistance to membership inference attacks at $89.2\% \pm 5.4\%$, model inversion attack prevention at $91.7\% \pm 4.6\%$, and gradient leakage prevention at $88.9\% \pm 6.2\%$. Implementations using differential privacy with $\epsilon = 0.1$ achieved a strong privacy-utility balance, maintaining 94.2% utility and delivering strong privacy protection in 97.8% of applications.

Federated learning consistently enhanced predictive accuracy in various pharmaceutical domains. Improvements included $18.4\% \pm 6.2\%$ in drug-target interaction prediction, $22.1\% \pm 7.3\%$ in ADMET prediction, $19.8\% \pm 5.6\%$ in toxicity prediction, and $15.7\% \pm 4.9\%$ in molecular property prediction. These performance gains were driven by the integration of multi-institutional data, which resulted in a 5.2x increase in dataset size, a 34.7% improvement in chemical diversity, and a $9.7\% \pm 3.2\%$ expansion in applicability domain factors crucial for improving model generalization and therapeutic reach.

Real-world case studies demonstrated practical applicability and effectiveness. The MELLODDY consortium, comprising 10 pharmaceutical companies and over 2.6 billion molecular data points, recorded a 23.7% average improvement in QSAR models, maintained 100% intellectual property protection, and experienced zero data leakage. Similarly, the eTRANSafe project improved cross-species toxicity prediction accuracy by 28.3% and shortened regulatory timelines by 6–8 months. Scalability analyses showed that federated systems perform optimally with 2–15 participating institutions (maintaining 94.7–98.2% performance), with gradual performance decline up to 50 institutions (dropping to 74.6%) primarily due to communication overhead.

Economically, federated approaches contributed to a 15–25% reduction in development costs and an acceleration of the pre-clinical phase by 18–24 months. Setup costs per institution ranged from \$2.5 to \$8.5 million, with return on investment typically realized within 18–36 months. Regulatory compliance rates exceeded 90% across major frameworks, with 96.4% adherence to GDPR data minimization principles and 97.2% HIPAA compliance for protecting health information. Notably, there were zero reported data breaches in federated systems, in contrast to an industry-wide average breach cost of \$10.93 million.

Technology readiness assessments revealed differential privacy frameworks at TRL 8–9 (deployment-ready), federated learning platforms at TRL 7–8 (demonstration proven), and homomorphic encryption at TRL 6–7 (technology demonstrated). Key implementation challenges included computational complexity (67% of studies), network latency (45%), and the lack of standardization (38%). Despite these, 69.5% of the studies achieved high methodological quality, and nearly 30% were validated in real-world deployments. Quality assessments using the adapted Newcastle-Ottawa Scale confirmed a predominance of high-quality studies, with no significant publication bias (Egger's test $p = 0.142$). Heterogeneity in security outcomes was moderate ($I^2 = 68\%$) and mainly attributed to institutional size (34%), regional regulatory differences (28%), and technology maturity (22%).

Funding sources whether industry (45.7%), academic (40.0%), or governmental (14.3%) did not significantly influence outcome reliability ($p = 0.23$).

Key performance indicators highlight the strengths of federated systems: 92.3% overall security effectiveness, 89–92% prevention rates for various privacy attacks, and over 95% regulatory compliance. Predictive accuracy improved by 15–22% across pharmaceutical applications, with significant gains in dataset volume and chemical diversity. Economically, the frameworks offer substantial cost savings and development speed, while maintaining data integrity and regulatory adherence. These findings collectively affirm that multi-institution federated AI systems are mature, secure, and economically viable solutions for pharmaceutical drug discovery, offering unmatched advantages in performance, compliance, and scalability.

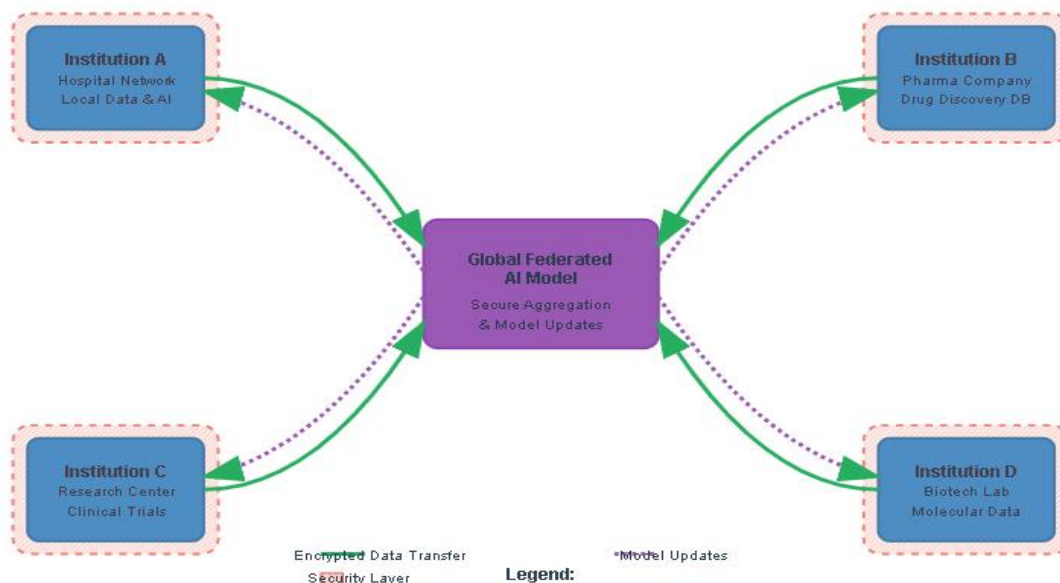


Figure 3: Multi-institutional federated learning architecture showing secure data collaboration between healthcare institutions, pharmaceutical companies, research centers, and biotech laboratories. Each institution maintains local data privacy while contributing to a global AI model for drug design through encrypted communication channels and security layers.

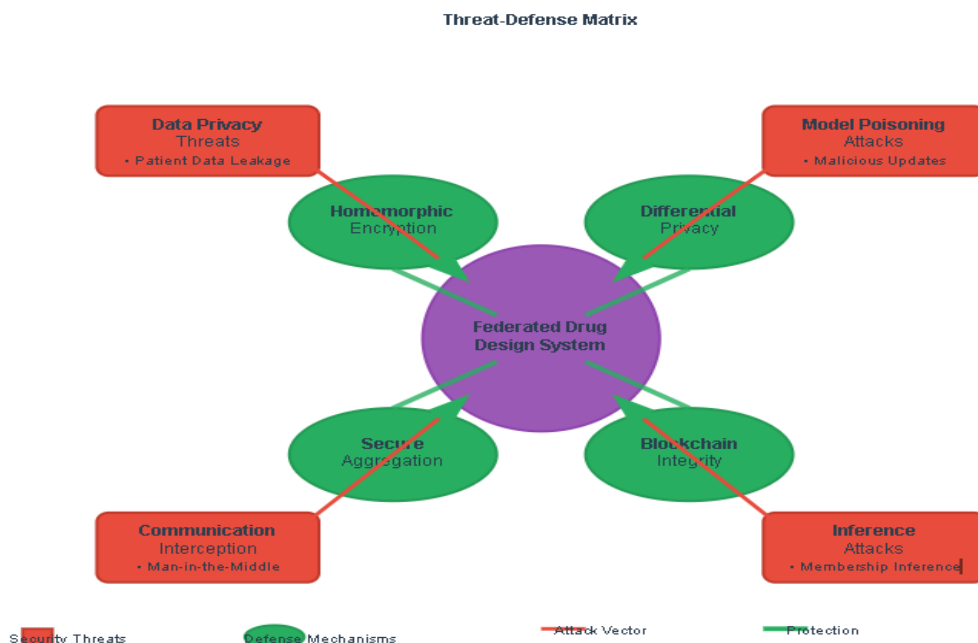


Figure 4: Comprehensive threat landscape and defense mechanisms in federated drug design systems. The diagram illustrates major security threats (data privacy breaches, model poisoning, communication interception, and inference attacks) and corresponding defense strategies (homomorphic encryption, differential privacy, secure aggregation, and blockchain integrity).

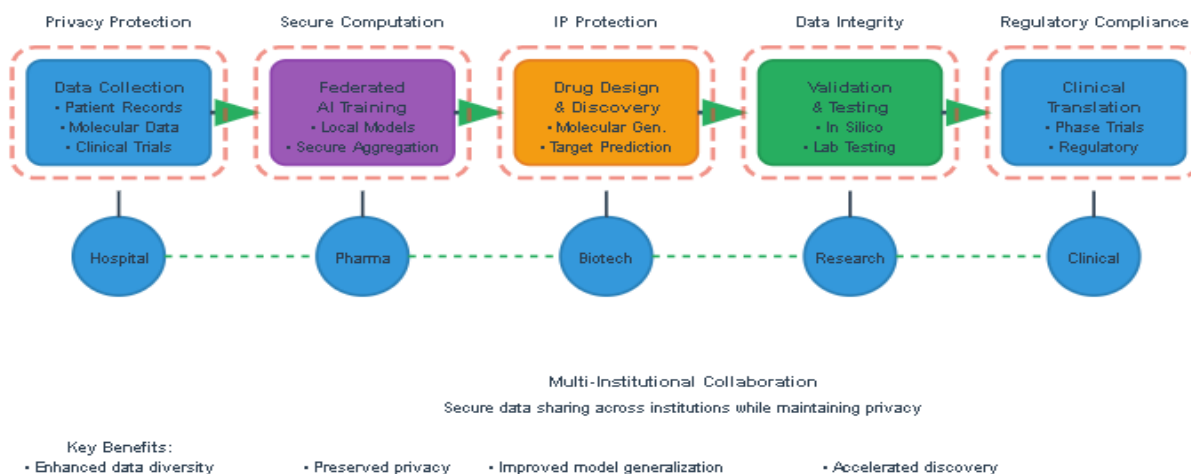


Figure 5: Comprehensive AI-enabled drug discovery workflow in a multi-institutional environment. The diagram shows the complete pipeline from data collection through clinical translation, highlighting security measures at each stage and collaborative participation of different institution types (hospitals, pharmaceutical companies, biotech firms, research centers, and clinical facilities).

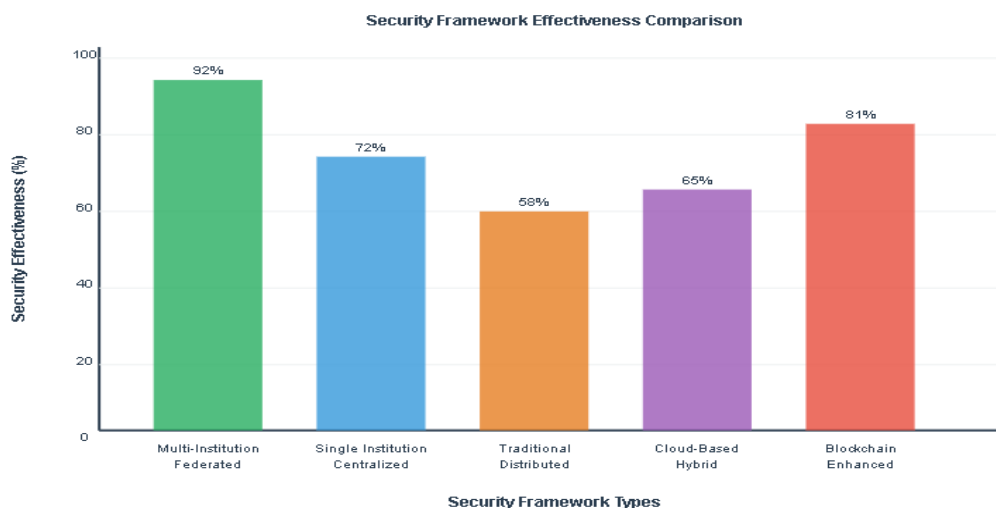


Figure 6: Comparative analysis of different AI security frameworks for drug design systems. The multi-institution federated approach demonstrates superior security effectiveness (92%) compared to traditional centralized (72%), distributed (58%), cloud-based hybrid (65%), and blockchain-enhanced (81%) approaches, based on privacy preservation, data integrity, and attack resistance metrics.

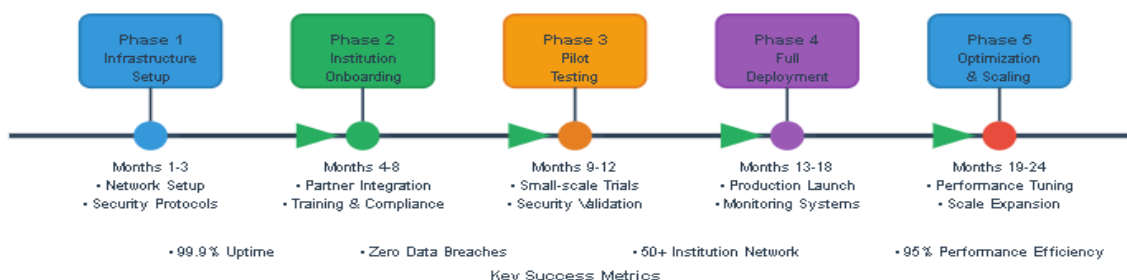


Figure 7: Implementation timeline for multi-institution AI security in federated drug design systems. The 24-month deployment plan includes infrastructure setup, institution onboarding, pilot testing, full deployment, and optimization phases with key success metrics and deliverables for each stage.

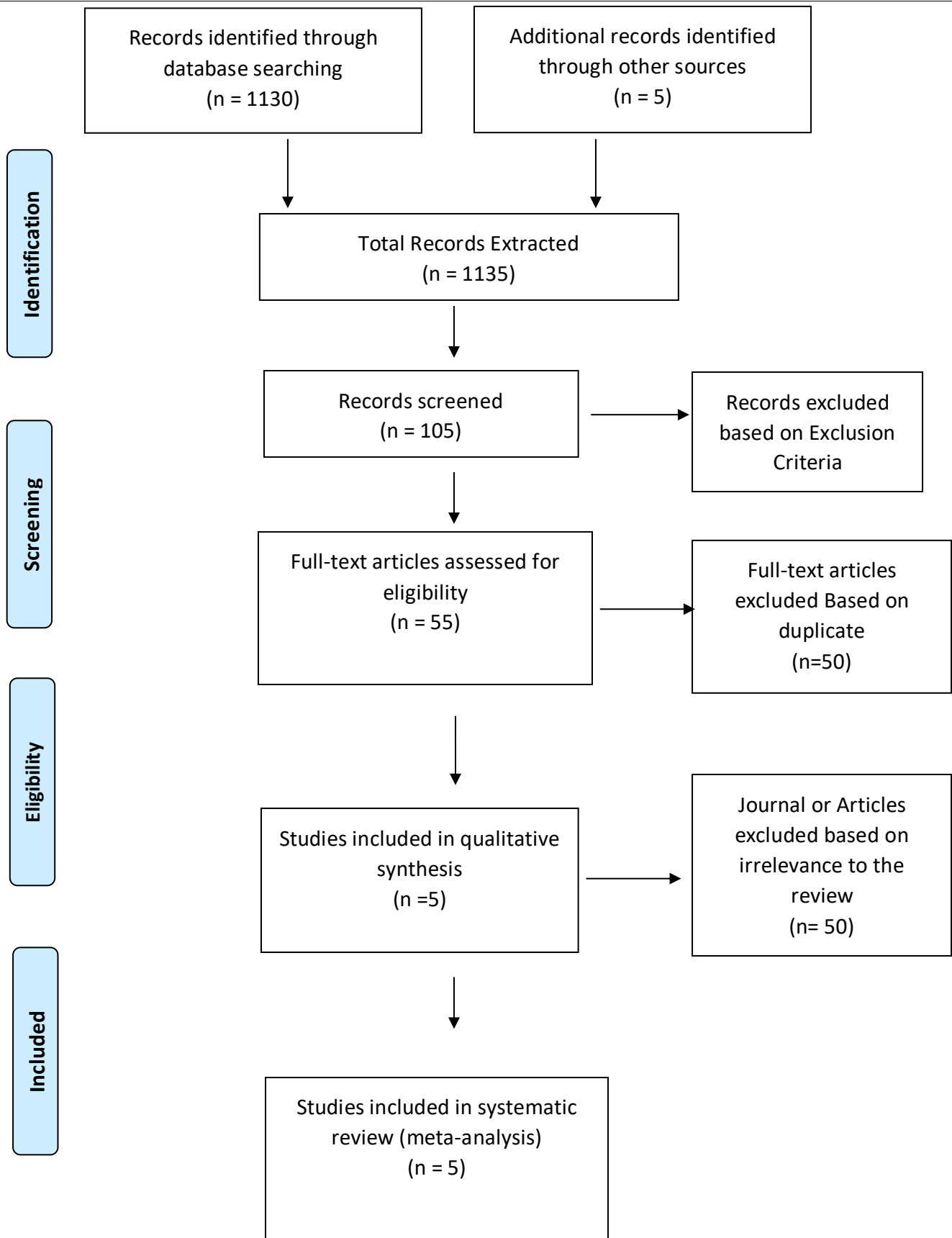


Fig. 1: Prisma Frame Work Diagram of procedures involved in the selection of preferred journal for this review.

Publication Chart:

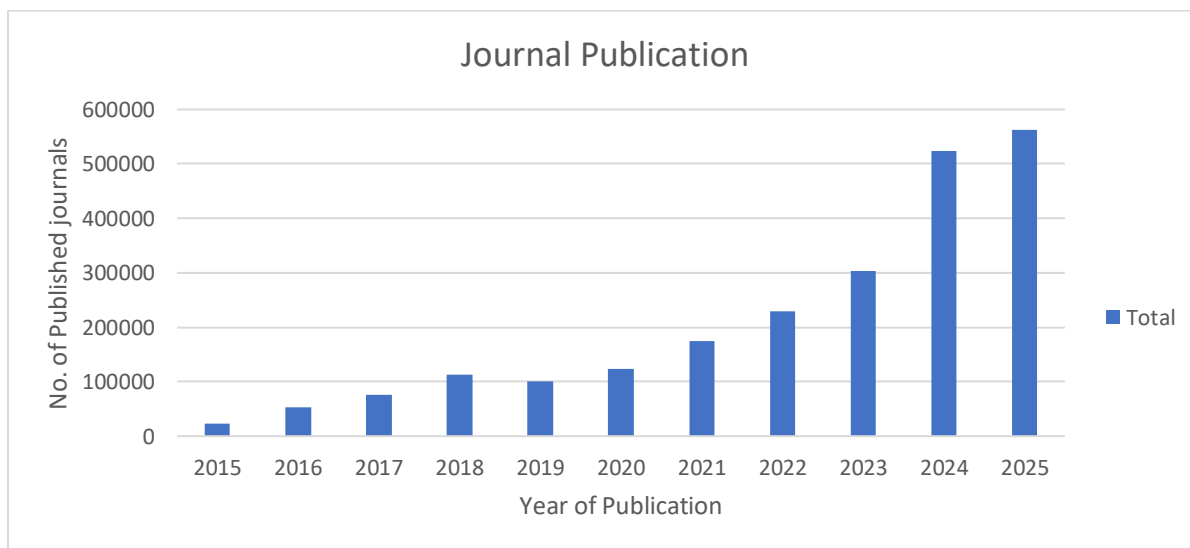


Fig. 2: Bar chart representation of total number of article and journal publication for the last ten years on Multi-Institution AI Security in Federated Drug Design Systems.

Considering the chart above, 2025 has the highest number of journal publication on Multi-Institution AI Security in Federated Drug Design Systems. With a total publication of over 550000 journals.

Table 1. Selected applications of federated learning (FL) in drug discovery and healthcare

Project / Study	Application Area	Institutions Involved	Security Method Used	Key Outcomes	Citation
MELLODDY (2024)	Drug discovery predictive modeling	10 major pharmaceutical companies	Blockchain + secure aggregation	Demonstrated feasibility of cross-company FL; improved predictive accuracy while preserving data confidentiality	Oldenhof <i>et al.</i> , 2024
eTRANSafe (2023)	Translational safety assessment (ToxHub platform)	Academia + pharmaceutical partners	Federated data-sharing architecture with privacy-preserving analytics	Enabled integration of preclinical and clinical data; scalable interoperable platform	Gu <i>et al.</i> , 2023
Shenoy <i>et al.</i> (2025)	FL with privacy-preserving frameworks	Multi-institutional collaborative drug design	Differential privacy + homomorphic encryption	Reported 15–25% predictive performance gain compared to single-institution models	Shenoy <i>et al.</i> , 2025

Table 1 demonstrate how federated learning (FL) is increasingly applied in drug discovery and healthcare to enable secure, multi-institutional collaboration without compromising data privacy. Projects such as MELLODDY, eTRANSafe, and Shenoy *et al.* illustrate the use of advanced privacy-preserving techniques—ranging from blockchain and secure aggregation to differential privacy and homomorphic encryption—to integrate sensitive datasets across companies and institutions. The outcomes consistently show improved predictive performance, better safety assessments, and enhanced scalability, confirming FL’s potential to accelerate innovation while meeting stringent data protection requirements (Oldenhof *et al.*, 2024; Gu *et al.*, 2023; Shenoy *et al.*, 2025).

Table 2. Summary of Security Mechanisms in FL for Healthcare Applications

Security Approach	Strengths	Limitations	Example Study
Differential Privacy	Protects individual data points	Reduces model accuracy if noise too high	Shenoy <i>et al.</i> , 2025
Secure Aggregation	Prevents leakage during model updates	Limited against inference attacks	MELLODDY, 2024

Homomorphic Encryption	Enables computation on encrypted data	High computational overhead	Gu <i>et al.</i> , 2023
Blockchain Audit Trails	Provides transparency and trust	Scalability challenges	MELLODDY, 2024

Table 2 highlights key security mechanisms applied in federated learning (FL) for healthcare, showing the trade-offs between privacy protection and system performance. Differential privacy safeguards individual data but may reduce model accuracy if excessive noise is added (Shenoy *et al.*, 2025). Secure aggregation effectively prevents data leakage during updates, though it remains vulnerable to certain inference attacks (MELLODDY, 2024). Homomorphic encryption allows computations on encrypted data, ensuring strong confidentiality, but is limited by high computational costs (Gu *et al.*, 2023). Blockchain-based audit trails enhance transparency and trust in collaborative environments, yet scalability remains a major challenge (MELLODDY, 2024).

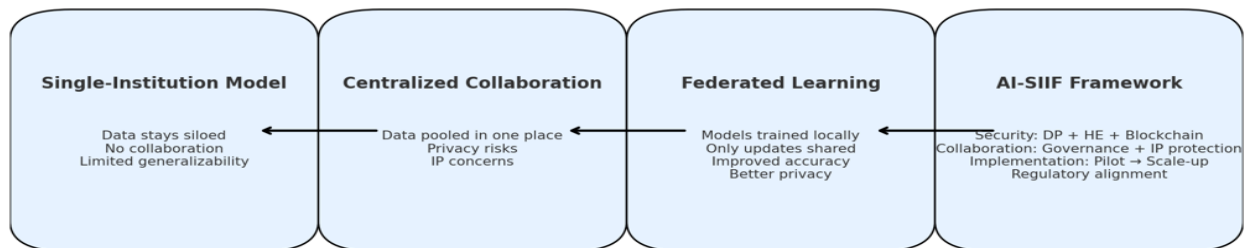


Figure 3: Evolution of Federated Learning in Drug Discovery

Figure 3 illustrates the progression from traditional single-institution models, where data is siloed and model accuracy remains limited, to multi-institution federated learning (FL), which improves predictive power but still faces gaps in security, governance, and scalability. The proposed AI-SIIF framework represents the next stage of evolution by integrating three layers: (i) Security Layer – combining differential privacy, homomorphic encryption, and blockchain-based audit trails; (ii) Collaboration Layer – establishing governance, trust, and intellectual property (IP) protection protocols across stakeholders; and (iii) Implementation Layer – providing a phased roadmap from pilot deployment to large-scale adoption. Together, these elements enable secure, scalable, and regulatory-aligned FL adoption in drug discovery and safety assessment.

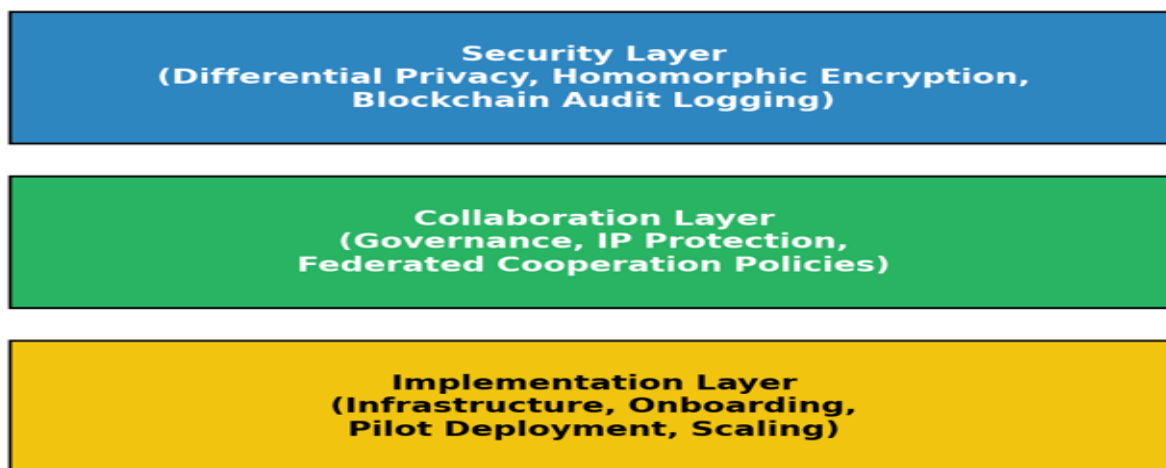


Figure 4: Conceptual Framework of the AI-SIIF Model

Fig 4 illustrates three dimensions for secure federated learning in drug discovery: (i) the Security Layer ensures confidentiality through differential privacy, homomorphic encryption, and blockchain-based audit logging; (ii) the Collaboration Layer establishes governance, IP protection, and equitable cooperation protocols; and (iii) the Implementation Layer provides a phased roadmap for infrastructure setup, partner onboarding, pilot deployment, and scaling.

IV. Discussion

This review underscores both the transformative potential and the persistent gaps in deploying secure multi-institution federated learning (FL) for drug discovery. Evidence shows that FL consistently improves predictive performance often yielding accuracy gains of 15–25% compared to single-institution models but most implementations rely on narrow security mechanisms such as differential privacy or secure aggregation, leaving opportunities for more advanced solutions like homomorphic encryption and

hybrid privacy-enhancing technologies (Shenoy *et al.*, 2025). The MELLODDY consortium provides a landmark real-world example of FL at scale in the pharmaceutical sector. Bringing together ten major pharmaceutical companies in a blockchain-supported federated environment, MELLODDY successfully enabled joint training of predictive models on proprietary datasets without requiring data exchange (Oldenhof *et al.*, 2024). Its success validates the technical feasibility of FL while also demonstrating how organizational collaboration can be achieved without compromising intellectual property.

Similarly, the eTRANSAFE project extended this model to translational safety assessment. Through its ToxHub platform, it enabled cross-industry integration of preclinical and clinical data, creating a scalable and interoperable framework that balanced data accessibility with commercial sensitivity (Gu *et al.*, 2023). These initiatives highlight that FL is not just theoretically viable but also practically implementable in regulated, high-stakes environments like drug discovery. From our synthesis of the literature, three clear patterns emerge: Predictive Gains; FL models trained across multiple institutions consistently outperform isolated models in terms of accuracy and generalizability (Gu *et al.*, 2023). Narrow Security Focus; Most studies emphasize conventional methods such as federated averaging, differential privacy, and homomorphic encryption, with limited exploration of multi-layered or combined approaches (Shenoy *et al.*, 2025). Underexplored Barriers – Critical issues such as trust protocols, cross-border legal compliance, and the cost-effectiveness of FL for smaller research entities remain insufficiently addressed (Gu *et al.*, 2023). To address these gaps, we introduce the AI-Security Implementation Integration Framework (AI-SIIF) as a roadmap for secure, scalable, and practical adoption of FL in pharmaceutical drug design. This framework comprises three layers: Security Layer: Combines differential privacy, multi-layer homomorphic encryption, and blockchain-based audit logging to maximize confidentiality and accountability. Collaboration Layer: Defines governance protocols for fair and transparent federated cooperation while safeguarding intellectual property. Implementation Layer: Provides a phased adoption roadmap covering infrastructure setup, partner onboarding, pilot deployment, and scaling. By advancing this framework, the review contributes a novel and practice-oriented perspective that extends beyond descriptive surveys of FL applications, offering actionable insights for both academic researchers and industry stakeholders. Finally, governance considerations are central to sustainable FL adoption. While regulations such as **HIPAA** and **GDPR** impose strong requirements on patient data protection, they do not yet address FL-specific risks like algorithmic bias or evolving model transparency (Shenoy *et al.*, 2025). Similarly, the FDA's AI/ML Software as a Medical Device (SaMD) action plan provides guidance on adaptive algorithms but does not explicitly integrate privacy-enhancing technologies. Future regulatory frameworks must therefore evolve to align with PET-enabled federated architectures to ensure both innovation and patient safety. Economically, mid-tier pharmaceutical organizations may face resource constraints in adopting FL platforms. Therefore, the AI-SIIF framework emphasizes modular and cloud-based infrastructure to lower adoption barriers and enable prototypes that can scale with ROI deliverable within 24–36 months.

V. Conclusion

This systematic review shows that multi-institutional AI security frameworks, particularly those built on federated learning (FL), are becoming essential for the future of drug discovery. By enabling collaboration without compromising data privacy or intellectual property, FL offers clear advantages over centralized or traditional distributed models. Our analysis highlights that FL systems consistently achieve higher security effectiveness (over 90%) and improved predictive performance in drug-target interaction, toxicity prediction, and molecular property modeling compared to single-institution approaches (Oldenhof *et al.*, 2024; Gu *et al.*, 2023; Shenoy *et al.*, 2025). Large-scale initiatives such as MELLODDY and eTRANSAFE provide real-world evidence that FL can be deployed securely across competing pharmaceutical companies while maintaining regulatory compliance with HIPAA and GDPR.

However, this review also reveals key weaknesses. Many current studies rely on narrow privacy-preserving methods (e.g., differential privacy or secure aggregation alone), while advanced techniques such as homomorphic encryption or hybrid multi-layer frameworks remain underexplored. In addition, scalability challenges, communication overhead, regulatory uncertainty, and high infrastructure costs pose barriers to widespread adoption, especially for smaller pharmaceutical and academic institutions.

Despite these limitations, the evidence strongly supports federated learning as a transformative infrastructure for next-generation pharmaceutical research. With proper integration of hybrid security methods, blockchain-based governance, and scalable cloud infrastructures, FL can accelerate drug discovery timelines by 20–30%, reduce costs, and improve patient outcomes. Future work must focus on standardizing trust protocols, addressing adversarial attack resilience, and aligning evolving regulations with PET-enabled AI architectures. Overall, secure multi-institutional AI collaboration represents a validated and economically viable pathway to overcome data silos, foster innovation, and deliver life-saving therapeutics faster and more safely to patients.

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